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PEDIATRIC AND ORTHOPAEDIC SURGERY

DISCIPLINE

DIAGNOSIS AND TREATMENT OF SKIN HEMANGIOMAS IN CHILDREN

SUMMARY OF THE Ph.D.THESIS

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CONTENTS

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Hemangioma, child, intratumoral injection, Bleomycin, prospective study, conclusions

INTRODUCTION

Name the term "hemangioma" comes from latin, where "hemangio" means blood vessel haem-(αίμα) and the term-oma "means tumor-oma (-ωμα). Hemagioamas are different from other tumors of the skin in that they are biologically active, their growth and development as separate, independent of increasing infant and child .. Hemangioma development of chip hyperplasia, while the other concerns the hypertrophy of vascular tumors. The term defines a congenital hemangioma vascular tumors with different locations, which shows a maximum size at birth and who subsequently shows an important development immediately after birth (1). A very important feature of these tumors is the rapid postnatal growth and slow involution

next period of childhood, especially for infantile hemangiomas.Hemangiomas are the most common tumors of the baby during time tumor formation compared to any other. In the literature it is estimated that the incidence varies between 1-3% of all newborns, and finds that sometimes reaches 10% by the age of 5 years. Immediately after birth it can be seen that the frequency of cutaneous hemangiomas is ranging between l.l% - 2.6% and increases to 8-12% by the age of 1 year (1)

In literature, it seems that the frequency of angiomas is higher in children born prematur.Also in infants weighing less than 1500 grams at birth cutaneous hemangiomas incidence is 15.6% and it increases with decreasing birth weight, reaching 22.9% in neonates weighing less than 1000 grams. (2) Regardless of the literature, it is apparent that the frequency of hemangiomas is clearly in favor of females, with oscillations contained in a girls-boys ratio of 3-1 to 5-1.

Another finding in various studies show that angioamas are more common in children with lighter skin color, caucasian. The occurrence is sporadic hemangiomas in families, but the authors (Blei & al) (2) which shows that families were highlighted where transmission was autosomal dominant hemangiomas. Also it is found that when identical twins there is statistical evidence to present value, leading to the calculation of a probable risk of development of hemangiomas. Development of cutaneous hemangiomas are more distinct phases: a proliferative phase in the first year of life, a stationary phase that can last months or even years, after which hemangiomas are entering a phase of regression, no matter the tumor is treated or not. This involution of the hemangioma may take various degrees, from slight regression to a complete disappearance of this.In some cases remains a hallmark of cutaneous hemangioma of existence, represented by a scar pigmentation , principle , considers that approximately 50% of cutaneous hemangiomas regress completely up to the age of 5 years, 70% by the age of 7 years, and a few extend their period of involution by the age of 10-12 years (3). Surface hemangioma, its thickness and its volume is not found to influence the rate of involution. No anatomical location and their number did not influence the evolution of a hemangioma, each tumor manifesting separately even if they are present in the same patient.

Hemangiomas in children

Patients with vascular anomalies have long attracted the attention of physicians, but the inability to understand the etiology, pathology and manifestation of the various vascular anomaly generated confusion among centuries in their treatment.

Vascular tumors are among the most common birth defects and neonatal. A better understanding of various clinical characteristics is essential for the pediatrician, pediatric surgeon, plastic surgeon and dermatologist to choose the most advantageous regimen and give as realistic a prediction for each patient.

Unfortunately, vascular tumor's history is characterized by varied terminology (arbitrary and inconsistent range) still creates confusion and misunderstanding. Terms such as cherries, strawberries, Porto wine, salmon are very descriptive color giving useful information on using the definitions. But does not provide useful classifications leading to confusion, as lesions showing different patterns of development can have.

From another point of view, the lesions that are the same but have different characteristics located deeper in color can lead to confusion.

Understanding these vascular anomalies has been greatly facilitated by Mulliken and Glowacki proposed that biological classification system, dividing the anomalies in the vessels that are biologically active (hemangiomas) and those which are biologically inactive (vascular malformations). Until today renowned doctors rejected this simplistic classification that slowly gained the place that really works. It is easy for doctors to understand what is happening, I can explain it easier for patients and provides a database from which to start rational therapeutic plan.

This clear distinction between tumors allows the clinician and psychologist to advise parents and to prevent the proliferation of present tumor and consequences.

This concept is unfortunately not very well known, and therefore we see children with disfiguring vascular tumors because their parents were advised to wait patiently involution and this does not happen.

The purpose of this paper is to clarify the differences, to facilitate diagnosis, and present treatment options (some of us) regarding hemangiomas. The personal part begins with the presentation of the material and working methods with parts list and presentation traced the number of cases that worked, recorded and conclusive tables. The next chapter presents the results obtained by the analysis of the study group, using various statistical models to show whether these results are significant and can be extrapolated to the entire group of patients with cutaneous hemangiomas. Follows a chapter in which I presented the diagnostic methods used around the period of the study, methods used in our clinic and comparison with current methods and described by other studies.

Next we have presented and analyzed the results of intratumoral injection of Bleomycin, used in our clinic as the only way of treatment.I mention that some of the results were used by publishing in journals (Journal of Pediatrics) or communicated in various specialized medical congresses (Constanta, Timisoara).

Then show the advantages and disadvantages of this method compared with the surgical method that has been used very often so far, emphasizing the use of intratumoral injection as an alternative to the surgical excision.We presented data from cutaneous hemangiomas analysis in terms of histology.

The last chapter, one of the conclusions, summarizes a number of issues that I have felt more special that is less discussed in literature or over which they insisted, was in some aspects even news.General bibliography includes titles that I had the opportunity to consult and who have focused in addressing the research question and that gave me a database to which I refer throughout development study. I thank colleagues from the department of pediatric surgery of Constanta County Emergency Hospital who have assisted in this study, and colleagues from the department of laboratory investigations and radiological investigations

Finally, thank prof. Dr. Tica Constantine scientific leader of the thesis, to whose guidance I have received over the four years that I realized this sentence.

PERSONAL PART

1.Data collection:

In collecting the data necessary for the study we used the database of Pediatric Surgery and Orthopedics Clinic in Constanta County Emergency Hospital. I was a database of patients admitted to the clinic who were diagnosed with cutaneous hemangioma in the period 1 January 2006-31 December 2011. The study included a total of 115 patients. Data on these patients were noted in the special form established for this study, by me, and analyzed from as many points of view.

Thus we obtained data on neonatal history, investigations carried neonatal gestationara age, maternal age at the time of pregnancy, patient skin pigmentation, birth weight, surface hemangiomas, their number source environment (urban or rural), presence of associated malformations, enterior treatments used in clinical presentation, presence or development of complications (ulcers, necrosis).

2.Criteria for inclusion in the study

Patients were considered in this study were children who were diagnosed in our clinic by one of the five doctors of the clinic and was treated and watched as evolution in time by these pediatric surgery.Were included in the study group patients and presented to the clinic for the first time and which were documented by images or stories exact time of occurrence of cutaneous hemangiomas and their evolution until the presentation in our clinic.Have been useful for our study only patients who had cutaneous hemangiomas, regardless of the number or location.

3.Exclusion criteria from the study

There were not included in this study patients had hemangiomas located in areas other than skin structures.Also not consider children who have exceeded the age of 18 when they were presented in the clinic.Another exclusion criterion was getting incorrect information from the patient or caregivers about hemangiomas time of onset, duration and number of their evolution.Were not taken into account other vascular tumors, such limfangiomas.

4. Cutaneous locating of hemangiomas

To achieve this goal we used images of patients consisting of photographs taken by them, either to highlight the angioma, be made randomly, but who could appreciate the tumor as well as photos taken by me in the clinic or other colleagues . In order to achieve the clinical relevance of these pictures we used cameras Nikon L22 High resolute and LG 550.It was noted the number of patients attending the skin angioamelor to achieve correct framing them within a hemangioma 1-3, 4-6 over 6 hemangiomas and hemangiomas.In case of multiple hemangiomas this we

conducted a complete picture of them to calculate their total area and number, so that we can include in the study an average of hemangiomas both in terms of area and their number.

5.Skin pigmentation

Because exist data in the literature on the incidence of cutaneous hemangiomas by skin pigmentation, we found it is necessary to keep in mind and this parameter. I had to admit that it can be made an infallible measuring grid color, so we created a scale of shades with values between 1 and 4, which correspond to the following values: 1 very light skin pigmentation to 4 - pigmentation very dark skin.

6.Age appearance

This criterion is particularly important one because in all literature is considered that there are certain thresholds that are true milestones in the evolution or involution of hemangiomas.
To pursue this parameter we requested photos of patients to be very exact conjunction with age and the pictures taken in the clinic were rated very strictly by marking them with the exact date of performing to have a hemangioma timing control phase by age patient.

7.Cutaneous hemangiomas association with other diseases

The summary highlighting the patients included in our study we considered needs to allocate space for diseases that we find sometimes associated angioamelor that by tracking statistics to see if we conclude on their importance in the development and / or evolution angiomatoase vascular tumors. Thus in the literature are mentioned genitourinary malformations, cardiac, ophthalmic and neurological.

8,Bleomycin injection

We use the product bleomycin for made intratumorals injection Pharmaceutical: The product is in the form of ampoules of 15 mg lyophilized substance.Technique we developed these injections consisted in preparing injectable solution by dilution in15ml serum vial, thus obtaining a solution with dilution of 1mg/ml.Is injected under general anesthesia in percutaneous intralesional doses: 0.5 mg / kg in children less than one year, 5-10 mg / kg in children older than one year.Minimum dose is 4.5 mg/m2, 165-168 mg/m2 dose is toxic. Postinjectional

behavior: pressure dressing, minimum time between two injections is 2 weeks, control blood, count monitoring systemic and local effectsActual injection was performed with disposable plastic syringes of 20 ml vial dilution has taken place. Injection method was one discontinuous, from the periphery to the center of hemangiomas.

9.Treatment

Were recorded and noted all the treatment that patients have suffered, both before presenting to the clinic, and after the presentation in our department. We also recorded complications occurred during various treatments, whether they have been randomly either were induced by the treatment used. We considered that we can have a database that allows the comparison between different types of treatment and their effectivenes.

10.Paraclynical investigation methods

- Ultrasound, performed in the radiology department of the hospital to provide information on the size of cutaneous hemangiomas

- Computer tomography (CT) performed in the presence of hemangiomas of the head and neck to obtain information on the depth of hemangiomas and damage nearby organs or anatomical structures, especially in locating the infants in the tumor was located in the skull (to highlight the existence of hemangiomas "glove finger" that are present both extra-and intracranial)

- Color Doppler ultrasound were performed to highlight the characteristics of the tumor, its proliferation and its maturity. They are also useful to highlight the stage where they are hemangioma, regression or evolution.

- Nuclear Magnetic Resonance (NMR) to clarify the depth and damage structures jerul skin hemangiomas.Study methods used for the study group of patients were: clinical - 101 patients, CT-8 patients, ultrasound-three patients lab-2 patients, MRI - 1 patient

11.Data processing

One of the important issues related to this study was that there are a large number of data to be analyzed, so had established a unified database, which is accessible by using a specialized language.

I used this program in Microsoft Windows Excel, which generated a relational database between different tables to be linked to each other through the same keywords that can serve up their position in various charts and tables.

I also used the IBM SPSS Statistics 19 was necessary because statistical analyzes in order to ascertain whether the observed differences between the various parameters are statistically significant, and if so we can be in graphic results.Descriptive statistical methods such as frequency, mean, standard deviation, maximum and minimum values, etc., have been used to highlight the properties and characteristics of the studied group.

Personal results

Lot analysis.

1.Gender distribution

In the study that we have conducted thus obtained a sex distribution - 115 out of a total of 43 patients were male and 72 were female, Percentage that means a preponderance of females over the male 62.61% female to 37.4% male or female / male 1.67 / 1 (grafic1)In international studies in the literature that I read (4) there was a gender distribution of 2.4 females to 1 male, so more than double presence of hemangiomas in females compared with sex male, similar to hemangiomas in female preponderance in our study. Could not obvious why tumor vascular malformations such a predisposition towards females, but it remains clear that it is something that is found in all the works consulted. Various authors have tried to link angioamas higher frequency in female hormonal specificity parameters but with no relevance quantifiably .

2.Distribution by area of origin

Depending on the area of origin of the patient data obtained show me their presence almost equal for both urban as well as rural areas.
This parameter was chosen in the study to highlight if a patient living environment, living conditions, diet have relievanta in appearance, development, evolution and involution of hemangiomas. The result, namely relative equality cases show that the environment influences the development angioamelor not. (Table 1)

environment of origin

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Urban	54	47.0	47.0	47.0
	Rural	61	53.0	53.0	100.0
	Total	115	100.0	100.0	

Table 1 lot hemangiomas in patients depending on the environment of origin

3.Distribution by age

This parameter is very important in the research study group because, as noted in the general, hemangiomas have a specificity related to the occurrence and development and is interesting if you can make a predictability of their development depending on whether theyThe analysis of our data shows that the vast majority of hemangiomas are present in infants, percentage of 73.91% obtained showing the special character of the age in hemangioma development.It can be seen that with the grace period of 1 year risk of developing cutaneous hemangiomas greatly decreases in infant period are found only seventh among patients who develop tumor.
Aged over three years is a significant milestone, only one in ten patients will develop disease.
These data are consistent with the description made in this regard by various authors, eg Maria Rosa Cordisco get a study found that about 70-90% of hemangiomas occur during the first weeks of life after the occurrence rate drops significantly (4)

4.Anatomical area affected

To determine areas most commonly affected anatomic have focused data obtained in a Pareto chart. This is to show which elements have the greatest influence - in this case that the vast majority of hemangiomas affects skin areas located in the head and neck (51%). (Table 2).
It is noted as the percentage decreases, the rarest being affected areas at the genitals and abdomen.

Anatomical area affected

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Abdomen	3	2.6	2.6	2.6
	Head and neck	59	51.3	51.3	53.9
	legs	12	10.4	10.4	64.3
	upper limb	13	11.3	11.3	75.7
	Multiple	6	5.2	5.2	80.9
	genital	5	4.3	4.3	85.2
	thorax	17	14.8	14.8	100.0
	Total	115	100.0	100.0	

Table 2 cutaneous hemangiomas by anatomic segment affected

This distribution of hemangiomas is very important because depending on the area and the affected organ should consider requiring immediate treatment or therapeutic expectation.
This preponderance of head and neck damage zones therapeutic decision involves a carefully controlled because many vital organs are located at these levels.

In the literature it is found that the presence of vascular tumors is similar in different studies. Thus the above-mentioned author (4) found that neck and head are affected at a rate of 72.5%.

5.Age of onset

Looking by age we found that their appearance is predominant in the first month of life, which is distinguished as a percentage of 27.8% of patients have at birth and 52.2% will develop soon after birth in the first four weeks.

6.Skin pigmentation

We have seen during the progress of my study that although the equal age and similar conditions this personal family history and the number of patients presenting spider differs depending on skin pigmentation, most commonly afectatii patients being those with skin as pale.We obtained a 67.8% share of all hemangiomas present in patients with light skin and 8.7% in those with very light skin, basically meaning that 76.5%, ie over three quarters of patients who develop hemangiomas the color of the skin open and very open.In international literature I found reference to this issue through the analysis of different races dermis in a prospective study achievements in USA (4) in which they were enrolled a total of 1058 patients found that 68.9% of them were Caucasian and only 14.4% were Hispanic and 2.8% Afro-American, which would suggest that the presence of hemangiomas is even greater as dermis color is lighter.

7.Hemangiomas distribution according to clinical classification

In the study group we found that the skin hemangiomas are represented predominantly by the localized, so 66 of the 115 patients had localized tumors compared with other types of hemangiomas, which cumulatively do not exceed 50% of the total. Conclude that multiple hemangiomas are rare, and the segmentation and indeterminate tie.According to new clinical classification proposed by Chiller and colleagues (5) in 2002 to find that they have shown the presence of hemangiomas located in a total of 72% patients, 18% segmentation, 9% and 3% unspecified multifocal (multiple). It can be seen that the presence of localized hemangiomas is more than double the amount other together. The study was done by these authors on a total of 327 patients presented as outpatients. In 2006 Häggström and colleagues (6) found this in a study comprising 1058 patients a similar report with the aforementioned results OBTAINED Chiller and collaborators in four years ago. In 2009 R. Mattassi, D.A. Loose, M. Vagit and colleagues (4) published new data reveal a distribution of 66.8% of hemangiomas localized 13.1% of the segment,

16.5% of the indeterminate and 3.6% of multifocal (multiple). These data OBTAINED in ten years time, are similar to data obtained by me and suggest that regardless of changes diagnostic related parameters, conditions of life, food, etc, this distribution remains constant, uninfluenced.

8.Complications during evolution

In the case of my study group found that out of 115 patients complications occurred during evolution angioamelor in 12 cases, ie ten were the occurrence of ulcers and two in the presence of bleeding.Reporting of data from the literature we found that in 2008 a study conducted by Kilcline C, Frieden IJ (8) shows that a total of 24% of patients with hemangiomas will develop complications during their evolution. This indicates a superior presence of ulcer complications compared with rest complications compared to 5:1 in favor of the former.This report is important because it reveals that any complications in the population studied are not very serious and that auditory and especially overhead obstructions which may endanger life are extremely rare. Also been observed in the literature that there is a percentage that varies between 4% and 10% of complications in newborns (7). This is important because it shows that almost half of all complications, somewhere between a third and half of all cases occur immediately postpartum, which means that it is necessary foatre hemangiomas present in the newborn to be very carefully monitored to prevent complications, watch them having more serious than an infant or big kid.

9 Adjacent to the surgical treatment need

Regarding the need for forms of treatment we found that the group of patients studied, a total of nine cases requiring medication or local form of dressing. Of these new cases that required medication and one eight had segmental hemangiomas located. In studies we have found relief being published in prestigious international journals (8) we found data showing that patients with segmental hemangiomas are 11 times more likely to develop complications and eight times more likely to require some form of treatment than localized hemangiomas.

10.Family history of vascular tumors.

One of the parameters of the study was to see whether family history have pathological significance in the emergence and development angioamelor. The data obtained show that of the 115 cases of the study group in 99 of the patients were absent and there were 16 of them in family history. A study conducted in 2009 by authors R. Mattassi, DA Loose, M. Vagit take into consideration family history of vascular disease (4). They found that the percentage of 16.6% there is a history of

vascular lesions in the presence of family and of these 87.5% were hemangiomas. It looks like the batch analysis data obtained from our international inscriun between parameters of various vascular studies.

11. Obstetric history

In an attempt to find a correlation between the occurrence and development of cutaneous hemangiomas on the one hand and various stakeholders have taken into consideration the presence of obstetrical history as a factor of influence. The data obtained showed that out of 115 cases, 82 of them were absent this history and that the 33 cases were present.This percentage means that 71.30% and 28.7 are without history are history, which seems to be quite important in the emergence angioamelor predictability.R. Mattassi and D.A. Loose in their study (4) found that a proportion of 37.6% of patients with hemangiomas have a history of obstetric problems.

Hemangiomas' diagnosis into the study group

Analyses performed to confirm the diagnosis

In order to establish the exact diagnosis of hemangiomas in our study were used to investigate different ways, as shown in the table below (table 3).

Analyses performed to confirm the diagnosis

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Clinic	101	87.8	87.8	87.8
	Clinic+CT	8	7.0	7.0	94.8
	Clinic+Ecografic	3	2.6	2.6	97.4
	Clinic+Laborator	2	1.7	1.7	99.1
	Clinic+RMN	1	.9	.9	100.0

Total	115	100.0	100.0	

table 3 **analyses performed to confirm the diagnosis**

It can be seen that the net dominate with a share of over 80% clinical examination. This shows that a diagnosis of cutaneous hemangioma is especially clinically, without requiring additional investigational effort (Chart 1)

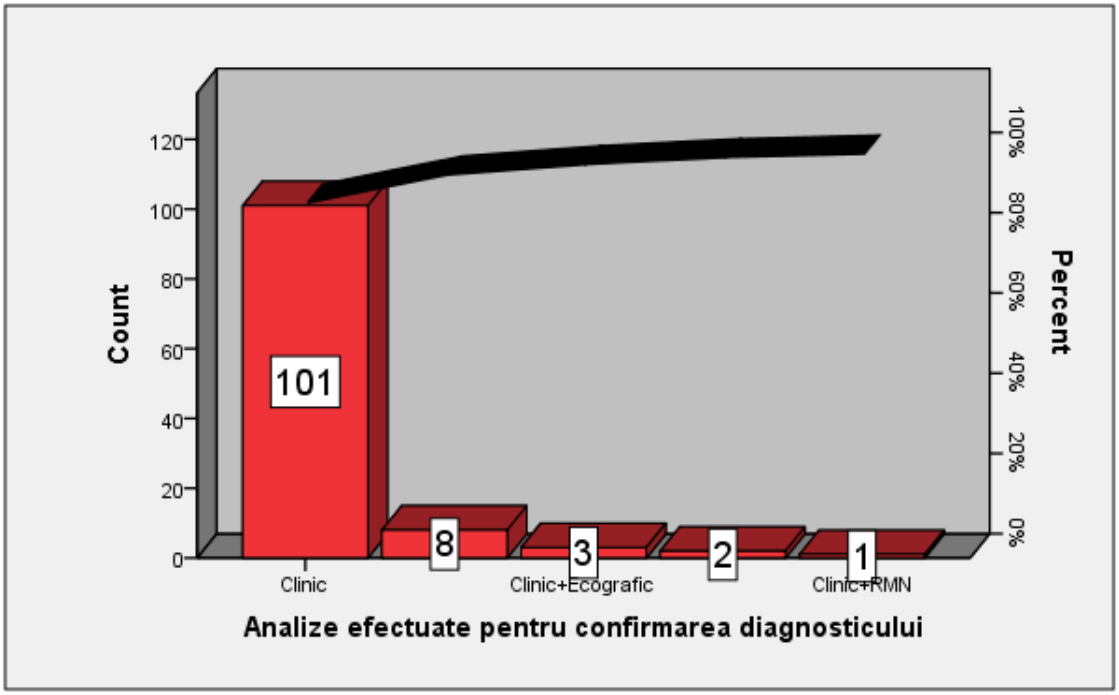

Chart 1. investigations required for diagnosis in our study

Given the importance of clinical diagnosis must show that if our group of study , clinical manifestations were varied.As follows:

- In the prodromal phase we found the occurrence of localized telangelectazii, circumcised or presence of lesions macula, dark blue. The differential diagnosis at this stage should pacut with: hemangioendoteliomul or congenital vascular malformations
- Proliferative phase occurrence of local hipercapilarization with increased skin thickness and mild exfoliationThe differential diagnosis at this stage is glomangiome hereditary, but they appear dark blue at birth

- Maturation phase is seen an important development of the vasculature, especially

of peripheral tumor volume and vascular proliferative appearance of peripheral color. The differential diagnosis at this stage is with other vascular malformations, but usually at this stage the clinical diagnosis is uncertain.
- Regression phase is found occurrence of capillaries with diffuse fibrosis discoloration of skin hyperpigmentation located.The differential diagnosis at this stage is done with other vascular malformation or vasculitis. In contrast, after this phase a proliferating hemangioma stop again.In the literature (1) I noticed how different authors also put great emphasis on clinical manifestation of cutaneous hemangiomas is considered a very safe method of diagnosis, which often is only required..As we noted in our group, used additional diagnostic methods to further investigate vascular tumor, the most useful were CT and ultrasound (simple or Doppler). In our activity we considered that an increase of 1-2 cm square surface hemangioma in a short period of time (several weeks) requires performing an ultrasound, which emphasize the development of cutaneous hemangioma.
In order to increase information about damage nearby organs and structures we considered necessary to make an MRI. Thoraco-abdominal ultrasound simply highlight structural changes of the affected area, but we have always done considering the comparative examination controlaterala normal anatomic structure.As shown in the picture below, an ultrasound is performed simple comparison in a patient MB aged 11 years admitted to our clinic with right lateral thoracic hemangioma, which highlights changes to the structure and thickness of the chest wall, left versus right. (Fig. 1)

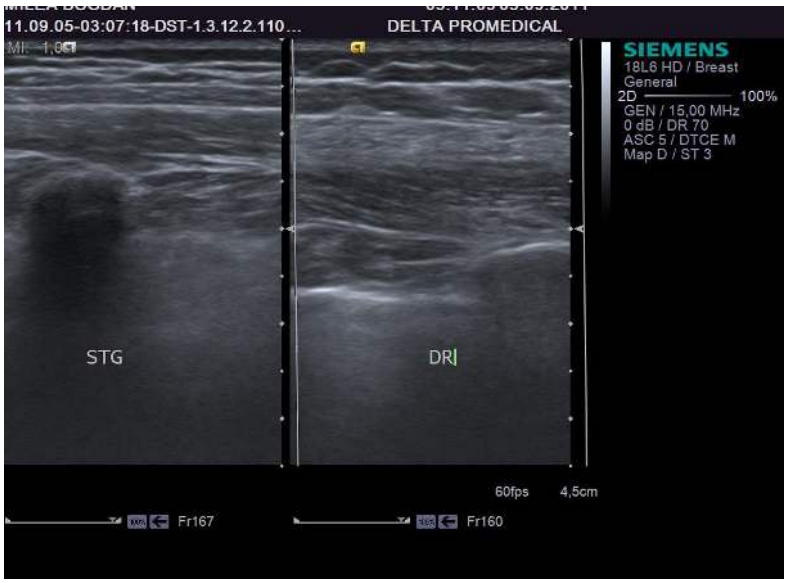

Fig. 1 simple thoraco-abdominal ultrasound.It find structural changes left versus right wall

To deepen this vascular tumor data we deciding to perform a Doppler ultrasound.
This examination provides enlightening information about hemangioma:

- Highlight its characteristics
- Determine proliferation
- Show maturity
- Indicate tumor regression or progression
- Highlight the evolution of overall tumor

Following this investigation performed in our clinic patient, note the slightly increased vascular density in the diffuse these muscle groups compared to normal towards the right. (Fig. 2)

Fig. 2 increased vascular density

Changes are present at significant distance from cutanata.Exemplu anomaly at distance of 8 cm cranial to the pigmented area stands out a bowl originating from subcostala arch, highly turbulent, with a diameter of 3 mm, which plans dicotomizeaza muscle. (Fig . 3)

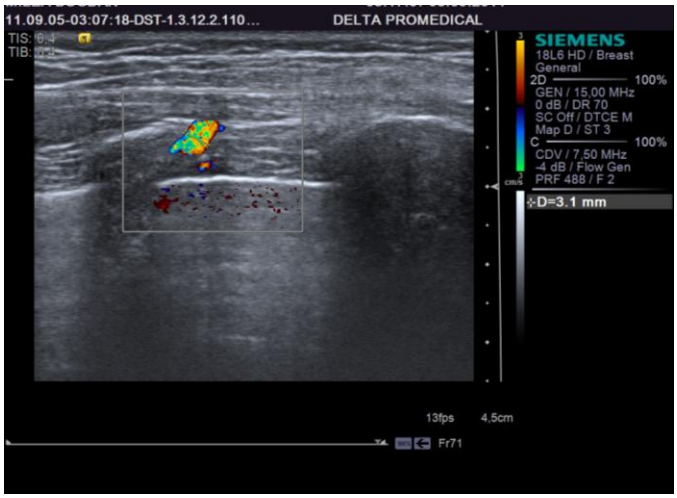

Fig . 3 hemangioma vasculature, the presence of underribb arch vessel

Following these imaging tests are disseminated vascular anomalies pulsed Doppler flow pattern suggesting the presence of arteriovenous communications miltiple with

consecutive muscle hypertrophy.To clarify the diagnosis further investigation is deemed necessary in that they perform an MRI examination of soft tissue dye. Following this laboratory examination shows the following: Posterior chest wall asymmetry, the right being more prominent by increasing the thickness of the subcutaneous layer (which measures 3 cm in the anterior-posterior direction). (Fig.4)

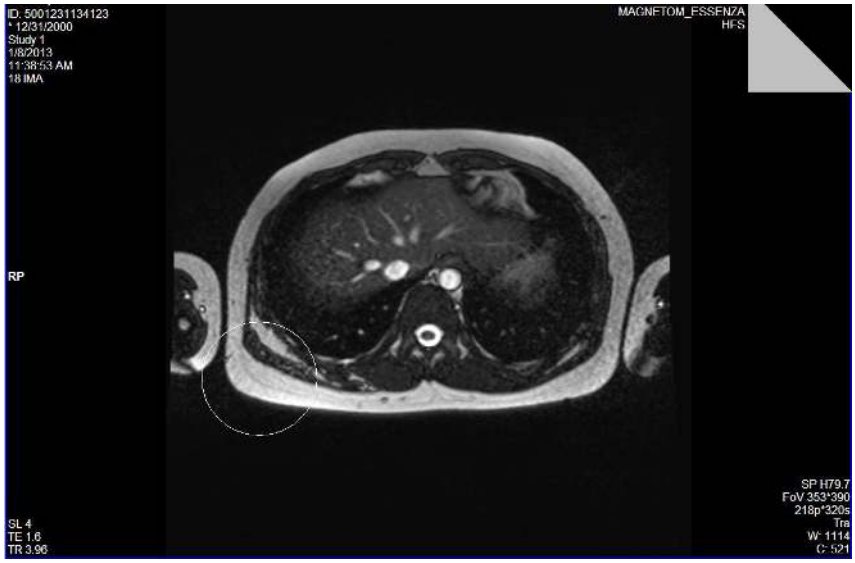

Fig.4 asymmetry posterior chest wall, posterior thoracic wall right (marked in circle) is thicker than the left

Parietal asymmetry extends over a length of about 20 cm, as can be seen from the picture below (Fig. 5).

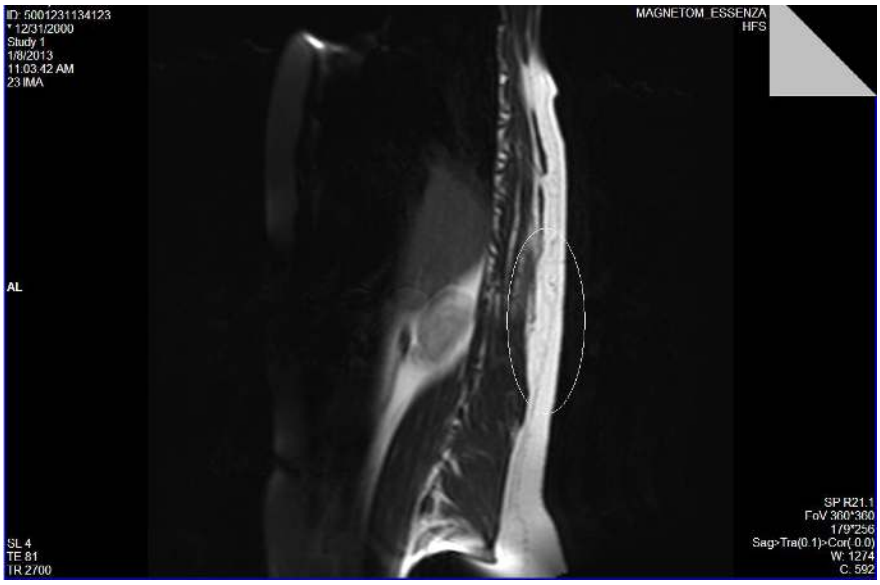

Fig. 5 MRI appearance , longitudinal section that shows cranio-caudal size of the hemangioma (marked in circle)

This associated present in the skin of a fine posterior hemithorax networks a small diameter vessels, cranial-caudal stretched over a length of 10 cm.
It is powered by a few tracks that cross vascular subcutaneous layer and muscle latissimus dorsi and is anastomosed with a network of small vessels located deep between muscles toothed -anterior and latissimus dorsi- posterior.
Deep vascular network has a diameter of 12 cm cranio-caudal and anastomosed with intercostal and paravertebral vascular branches.This network highlighted vascular magnetic resonance, as shown in the figure below, comes to confirm and complete Doppler ultrasound data, which identifies itself with this communication arterio - venous. (Figure 6)

Figure 6 anastomosis between dermal vessels of hemangioma and vascular network branches intercostal and paravertebral (area marked in circle)

The conclusions of these complex investigations lead to the establishment of the diagnosis with certainty "capillary hemangioma located in the deep and superficial posterior wall of the right hemithorax."

Bleomicina treatment of the study group

1.Bleomicina

Intratumoral injection of Bleomicina has been used in our study as a unique method of therapy.

Although the product is used mainly in medicine for cytostatic effect in achieving the therapeutic effect of these substances on vascular tumors have taken into account the side effect of its injection, namely the determination of a significant vascular sclerosis.

Overview (fig. 7)

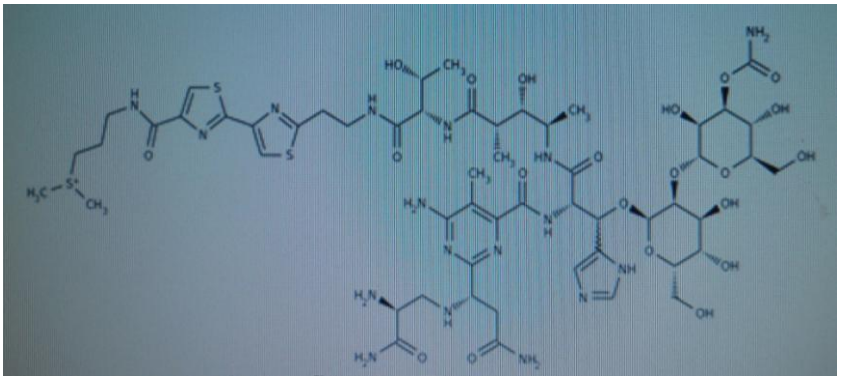

fig. 7 Bleomicina biochemical formula

(3-{[(2'-{(5S,8S,9S,10R,13S)-15-{6-amino-2- [(1S)-3-amino-1-{[(2S)-2,3-diamino-3-oxopropyl]amino}-3-oxopropyl] -5-methylpyrimidin-4-yl}-13-[{[(2R,3S,4S,5S,6S)-3- {[(2R,3S,4S,5R,6R)-4-(carbamoyloxy)-3,5-dihydroxy-6- (hydroxymethyl)tetrahydro-2H-pyran-2-yl]oxy} -4,5-dihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl]oxy} (1H-imidazol-5-yl)methyl]-9-hydroxy-5-[(1R)-1-hydroxyethyl]-8,10-dimethyl-4,7,12,15-tetraoxo-3,6,11,14-tetraazapentadec-1-yl}-2,4'-bi-1,3-thiazol-4-yl)carbonyl]amino}propyl)(dimethyl)sulfonium

Bleomicina is a glycopeptide antibiotic produced by the bacterium Streptomyces verticillus.

Bleomicina containing the Bleomicin sulfate like active substance. Bleomicina belongs to a group of drogs called chemotherapy. These drugs, is used for cancer chemotherapy.

2Annual distribution of patients

Patients who were treated in our clinic by injection of Bleomycin, as only method of treatment was 115 children.

Distribution by year was:

- 2006: 18 patients
- 2007: 18 patients
- 2008: 22 patients
- 2009: 31 patients
- 2010: 19 patients
- 2011: 7 patients

3Number hemangiomas / patient

One of the most important parameters in the study was the number of hemangiomas present for each patient.

The classification was made keeping in mind not the surface of each hemangioma but strictly for their number as shown in the chart below.The data obtained were:

- Single hemangioma - 105 patients
- Between 1si 6 hemangiomas - 8 patients
- Over 6 hemangiomas- 2 patients

In percentage terms it is found that over 90% of patients have a single hemangioma, In specialized studies by other authors find that percentage by number hemangiomas present identified the following situation: 75% of total hemangiomas are single lesion, 23% of them are with a number of injuries between three and six and only 2% of hemangiomas is manifested by the presence of over six injuries (4).

4.Number injections of Bleomicina

Because the treatment was only performed intralesional injection I was interested in calculating the number of injections required to achieve the main objective of treatment - healing.The number of injections per patient ranged was from one to six, most patients requiring two, three or four injections to achieve our goal. In percentage terms we find that in the main, that 37% of cases required three injections, 34% two and 20% four remaining patients requiring different management, but in much smaller proportions.

5 Posttreatment complications

To analyze the body's response to intratumoral injection of bleomicina I watched the final output and complications that may occur during treatment. In this context we noted the appearance of hyperpigmentation scars where the 31 patients of the 115, the remaining 84 without any problem of complication. It turns out that three quarters of those blomicina infiltration was very good, without the occurrence of complications and only a quarter of patients have evolved with the presence of hyperpigmentation scars.

6.Days of hospitalization

This was important in our study considering two aspects:
- Patient comfort, who wants a more rapid return to the family and loading with patients of the department .Predominated patients required hospitalization for three and two days, according to the mean number of injections was predominantly three.

Comparative study between surgery excision and injection with bleomycin to cutaneous hemangiomas in children

For a better building of advantages or disadvantages of treatment with intralesional injection of bleomicina , compared to other methods, I did comparing the evolution of hemangiomas after their surgery treatment done in our clinic. I was interested in two important parameters namely : healing time and the second parameter was the clinical outcome. We felt that these parameters are the most important because we took into account the parents' requests for clarifying that at the first consultation want to know how long it will take treatment, how many injections will be needed if it is better to a classic surgical method and after how many injection with Bleomicina

tumor will dissapear.You must keep in mind that mostly affected regions of the head and neck regions that are highly visible, which can not be covered by clothes and remaining exposed to the gaze.The treatement what we propose to the parents must meet two criteria: treatment with reducing the likelihood of tumor recurrence and this aesthetic criterion, criterion very important for tutors .If we compare the surgical excision versus bleomycin injection of hemangiomas can be seen that the first method has the advantage of time-is done immediately, the patient evecte visible and immediate caregivers, it requires multiple repetitions, is unique, and quite often require reintervention .But you should note that although it is faster and more limited financial resources, surgical excision has a major drawback, namely that it leaves behind scars postoperative depending on surgeon, his technique and patient dermstructure.Therefore we believe that injection of bleomycin is one approach superior to that excision because, despite the fact that a greater effort involves both doctor - repeated interventions,conviction patients and their caregivers to be patient, greater financial efforts (repeated interventions involving higher costs) and patient-multiple interventions, forward, has a great advantage, namely the lack of dermal scarring.In all injections that we conducted in clinical outcome dermal tissue was significantly higher than post-intervention excisional scar and slightly brownish color of the skin is net of any favorable postoperative scarring.We can say that every effort for intralesional injection of bleomycin are rewarded by the final appearance of the skin and patient satisfaction.In the figure below (Figure 8) is presented a ten year old patient who was operated in our clinic for a laterocervical hemangioma , and after a six months postoperatively shows a significant keloid scars.We believe this scar could have been avoided if parents would not have opted for surgical excision treatment.

Figure 8 significant keloid scar at six months postoperatively

Histological study of hemangiomas

Histologically hemangiomas presents the following structure:

1.Hemangiomas simple: telangiectasia are present in the superficial dermis with well defined, flat, accompanied by redness of the skin and its elevation. Tumor.regresion is unlikely.

2. Hemangiomas in "salmon patches" characterized by significant dilatation of capillaries, redness strong, some with possible regression, some not, depending on their anatomical location.

3. Hemangiomas looking for "strawberry spots" are arranged in the form of strawberries, nodular tumor and their regression is staying with residual scarring skin.

4. Cavernous hemangiomas: are characteristic proliferation of small vessels in the deep dermis and usually have no spontaneous regression, evolving most often to increase.

Conclusions

1.Diagnosis of cutaneous hemangiomas

In terms of diagnosis and investigations I believe that the diagnosis is mainly clinical, within our group of 115 patients we established a diagnosis of certainty in the case of 101 patients, only the remaining 14 needing additional means of diagnosis, documentation (such as pictures), made by the doctor or patient having a significant role in determining the development and aggressivity of hemangioma. Doppler ultrasound has a role to complete the investigation, can determine the characteristics of angioma, its proliferation, degree of maturation, regression or state or evolution.Modern means of diagnosis of these tumors, means that we have applied in our clinic, such as CT, MRI, ultrasound, allowing a diagnosis of high acuity, which will be found in choosing the best treatment methods.

2.Frequency

The data obtained in the study can conclude that hemangiomas are benign tumors that are common in infants from birth to rare large explosion in the first months of life. This is very important for both physician and patient, because you can not make a prediction on the occurrence of hemangiomas in children, every newborn is a potential further developed by hemangioma. Skin color, pigmentation it is more important predictive role, we found that hemangiomas occur with predilection in patients with skin as pale and percentage decrease with increasing skin pigmentation, resulting in a preponderance of 87% of their people light skin and only 13% in people with darker skin color in the study that we conducted, so the ratio is one to nine people at the expense of those with lighter skin.

3. There is no universally accepted behavior on the timing of treatment.

In our clinic we chose to start treatment as soon as possible by intratumoral injection of Bleomicina due to the following reasons:

a) a regression hemangioma has indeed increased chance of 70% according to the literature, but 30% will regress and we shall not be specified on the basis of current knowledge of them will regress or not

b) 50% of hemangiomas of the head and neck are bringing significant aesthetic changes accepted hard by the parents, and the risk to grow progressively is high.

c) location: perioftalmic, buccal, nasal or holes require immediate action to prevent functional disorder of various equipment and systems.

Expectant treatment, observation of evolution or involution of hemangiomas can be adopted in their present locations in the lower limbs or upper trunk which grows not aggressively even if it would not be a danger to the patient aesthetically and functionally.We believe that should be considered urgent angioamas that develops on the face, perineum, arm or leg, or those with aggressive growth that doubles its size within two weeks, regardless of their location.

4. Age to start the treatment

Following our expierentei believe that age is not an impediment to starting treatment, subject to the sclerosing agent dosage 0.5 mg / kg that we used in our injections.

5.Adverse effects and complications

At this subject we must say that an important role in very little complication have the plasma concentration of bleomycin obtained after intratumoral injection of cutaneous hemangiomas , which is much lower compared to intravenous administration of the same substances in the treatment of neoplazic diseases. Even if treatment is achieved by multiple injections, spaced at intervals of time, usually three weeks, the net result is favorable to the surgery, even if rapid, can leave semnifivative skin scars.

6. Need medical interdisciplinary collaborations

A good interdisciplinary collaboration can lead to successful resolution of these vascular malformations , mutilating , a more rapid presentation of patients to specialized medical shorten the time of hemangioma develops and thus decreases the chance for it to cause a significant damage, sometimes irreversible, the aesthetic and / or functional with significant implications later in future adult life.

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